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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Treatments for Acute Pain: A Systematic Review

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Treatments for Acute Pain: A Systematic Review,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before 30 days after date of publication of this Notice.

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

Mail Stop 06E53A

Rockville, MD 20857
Shipping Address (FedEx, UPS, etc.):
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FOR FURTHER INFORMATION CONTACT: Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION: The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for Treatments for Acute Pain: A Systematic Review. AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Treatments for Acute Pain: A Systematic Review*, including those that describe adverse events. The entire research protocol is available online at: https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/protocol

This is to notify the public that the EPC Program would find the following information on *Treatments for Acute Pain: A Systematic Review* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.

- *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.

- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

Each Key Question (KQ) focuses on a specific acute pain condition. The conditions and related subquestions are listed below:

KQ1: Acute back pain (including back pain with radiculopathy)
KQ2: Acute neck pain (including neck pain with radiculopathy)
KQ3: Musculoskeletal pain not otherwise included in KQ1 or KQ2 (including fractures)
KQ4: Peripheral neuropathic pain (related to herpes zoster and trigeminal neuralgia)
KQ5: Postoperative pain after discharge
KQ6: Dental pain (surgical and nonsurgical after discharge)
KQ7: Kidney stones
KQ8: Sickle cell crisis (episodic pain)

For each condition above, the following subquestions will be addressed:

Opioid Therapy

a. What is the comparative effectiveness of opioid therapy versus: 1) nonopioidpharmacologic therapy (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, anticonvulsants) or 2) nonpharmacologic therapy (e.g., exercise, cognitive behavioral therapy, acupuncture) for outcomes related to pain, function, pain relief satisfaction, and quality of life and after followup at the following intervals: less than 1 day; 1 day to less than 1 week; 1 week to less than 2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?
b. How does effectiveness of opioid therapy vary depending on: (1) patient demographics (e.g. age, race, ethnicity, gender); (2) patient medical or psychiatric comorbidities; (3) dose of opioids; (4) duration of opioid therapy, including number of opioid prescription refills and quantity of pills used; (5) opioid use history; (6) substance use history; (7) use of concomitant therapies?

c. What are the harms of opioid therapy versus nonopioid pharmacologic therapy, or nonpharmacologic therapy with respect to: (1) misuse, opioid use disorder, and related outcomes; (2) overdose; (3) other harms including gastrointestinal-related harms, falls, fractures, motor vehicle accidents, endocrinological harms, infections, cardiovascular events, cognitive harms, and psychological harms (e.g., depression)?
d. How do harms vary depending on: (1) patient demographics (e.g., age, gender); (2) patient medical or psychiatric comorbidities; (3) the dose of opioid used; (4) the duration of opioid therapy; (5) opioid use history; or (6) substance use history?
e. What are the effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on 1) short-term (<3 months) continued need for prescription pain relief, such as need for opioid refills, and 2) long-term opioid use (3 months or greater)?
f. For patients with acute pain being considered for opioid therapy, what is the accuracy of instruments for predicting risk of opioid misuse, opioid use disorder, or overdose?
g. For patients with acute pain being considered for opioid therapy, what is the effectiveness of instruments for predicting risk of opioid misuse, opioid use disorder, or overdose?
h. For patients with acute pain being considered for opioid therapy, what is the effect of the following factors on the decision to prescribe opioids: (1) existing opioid management plans; (2) patient education; (3) clinician and patient values and preferences related to opioids; (4) urine drug screening; (5) use of prescription drug monitoring program data; (6) availability of close followup?

Nonopioid Pharmacologic Therapy

i. What is the comparative effectiveness of nonopioid pharmacologic therapy (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, anticonvulsants) versus: 1) other nonopioid pharmacologic treatments, such as those in a different medication class; or 2) nonpharmacologic therapy for

outcomes related to pain, function, pain relief satisfaction, and quality of life after followup at the following intervals: <1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

j. How does effectiveness of nonopioid pharmacologic therapy vary depending on: (1) patient demographics (e.g. age, race, ethnicity, gender); (2) patient medical and psychiatric comorbidities; (3) the type of nonopioid medication; (4) dose of medication; (5) duration of treatment?

k. What are the harms of nonopioid pharmacologic therapy versus other nonopioid pharmacologic therapy, or nonpharmacologic therapy with respect to: (1) misuse, (2) overdose; (3) other harms including gastrointestinal-related harms, cardiovascular-related harms, kidney-related harms, falls, fractures, motor vehicle accidents, endocrinological harms, infections, cognitive harms, and psychological harms (e.g., depression)?

l. How do harms vary depending on: (1) patient demographics (e.g. age, gender); (2) patient medical comorbidities; (3) the type of nonopioid medication; (4) dose of medication; (5) the duration of therapy?

Nonpharmacologic Therapy

m. What is the comparative effectiveness of nonpharmacologic therapy versus sham treatment, waitlist, usual care, attention control, and no treatment after followup at the following intervals: less than 1 day; 1 day to less than 1 week; 1 week to less than 2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

n. What is the comparative effectiveness of nonpharmacologic treatments (e.g. exercise, cognitive behavioral therapy, acupuncture) for outcomes related to pain, function, pain relief satisfaction, and quality of life after followup at the following intervals: less than 1 day; 1 day to less than 1 week; 1 week to less than 2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

o. How does effectiveness of nonpharmacologic therapy vary depending on: (1) patient demographics (e.g. age, gender); (2) patient medical and psychiatric comorbidities?

p. How do harms vary depending on: (1) patient demographics (e.g. age, gender); (2) patient medical and psychiatric comorbidities; (3) the type of treatment used; (4) the frequency of therapy; (5) the duration of therapy?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings)

Picots Element	Inclusion Criteria
Population	Adults with acute pain related to the following conditions: 1. Acute back pain (including back pain with radiculopathy) 2. Acute neck pain (including neck pain with radiculopathy) 3. Other musculoskeletal pain 4. Peripheral neuropathic pain (related to herpes zoster and trigeminal neuralgia) 5. Postoperative pain after discharge 6. Dental pain 7. Kidney stones 8. Sickle cell crisis (episodic pain) *Special populations: ▪ General adult ▪ Older populations >65 years ▪ Patients with history of substance use disorder ▪ Patients currently under treatment for opioid use disorder with opioid agonist therapy or naltrexone ▪ Patients with a history of psychiatric illness ▪ Patients with history of overdose ▪ Pregnant/breastfeeding women ▪ Patients with comorbidities (e.g., kidney disease, sleep disordered breathing)
Interventions	**Opioid therapy:** a-e. Any systemic opioid, including agonists, partial agonists, and mixed mechanism opioids. f. Instruments, genetic/metabolic tests for predicting risk of misuse, opioid use disorder, and overdose g. Use of risk prediction instruments, genetic/metabolic tests h. The following factors: (1) existing opioid management plans; (2) patient education; (3) clinician and patient values and preferences related to opioids; (4) urine drug screening; (5) use of prescription drug monitoring program data; (6) availability of close followup **Nonopioid therapy:** Oral, parenteral, or topical nonopioid pharmacological therapy used for acute pain (acetaminophen, nonsteroidal anti-inflammatory drugs, skeletal muscle relaxants, benzodiazepines, antidepressants, anticonvulsants, cannabis). **Noninvasive nonpharmacological therapy:** Noninvasive nonpharmacological therapies used for acute pain (exercise [and related therapies], cognitive behavioral therapy, meditation, relaxation, music therapy, virtual reality, acupuncture, massage, manipulation/mobilization, physical modalities [transcutaneous electrical nerve stimulation, ultrasound, braces, traction, heat, cold])

Picots Element	Inclusion Criteria
Comparators	**Opioid therapy:** a-d. Usual care, another opioid, nonopioid drug, or noninvasive, nonpharmacological therapy e. Usual care, another opioid, nonopioid drug, or noninvasive, nonpharmacological therapy, no opioid/nothing prescribed f. Reference standard for misuse, opioid use disorder, or overdose; or other benchmarks g. Usual care h. Not utilizing the factors specified in interventions (h) above **Nonopioid pharmacological therapy:** Other nonopioid pharmacological therapy or noninvasive nonpharmacological therapy **Noninvasive nonpharmacological therapy:** Sham treatment, waitlist, usual care, attention control, and no treatment; or other noninvasive nonpharmacological therapy
Outcomes	**Opioid therapy:** a-d, g, i. Pain, function, pain relief satisfaction, and quality of life, harms, adverse events (including withdrawal, risk of misuse, opioid, opioid use disorder, overdose). e. Persistent opioid use f. Measures of diagnostic accuracy h. Opioid prescribing rates **Nonopioid therapy:** pain, function, pain relief satisfaction, quality of life and quality of life, harms, adverse events, opioid use **Noninvasive nonpharmacological therapy:** pain, function, pain relief satisfaction, quality of life and quality of life, harms, adverse events, opioid use
Time of followup	<1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to <4 weeks; ≥4 weeks
Setting	Emergency department (initiation of therapy and following discharge), physician's office, outpatient or inpatient surgical center, dental clinic or oral surgery center, inpatient (sickle cell only)
Study design	All KQs: RCTs; in addition: e. cohort studies (for long-term opioid use) f. studies assessing diagnostic accuracy h. cohort studies and before-after studies assessing effects on prescribing rates

Abbreviations: RCT = randomized controlled trial

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